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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,021	08/20/2003	Ming-Hui Wei	CL001201DIV	4849

25748 7590 04/24/2006

CELERA GENOMICS
ATTN: WAYNE MONTGOMERY, VICE PRES, INTEL PROPERTY
45 WEST GUDE DRIVE
C2-4#20
ROCKVILLE, MD 20850

EXAMINER	
CROWDER, CHUN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,021	WEI ET AL.	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 15-29* is/are pending in the application.

4a) Of the above claim(s) *1,2,28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3, 15-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

DETAILED ACTION

1. The examiner of this application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Chun Crowder, Group Art Unit 1644, Technology Center 1600.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

For example, eight sequences disclosed in Figures 2A, 2C, 2D and Figures 3O-3P of the specification. However, the sequences fail to comply with the Sequence Rules.

Applicant is reminded of the Sequence Rules which require a submission for all sequences of 10 or more nucleotides or 4 or more amino acids (see 37 CFR 1.1821-1.1825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules.

Applicant must comply with the requirements of the Sequence Rules (37 CFR 1.1821-1.1825) in response to this Office Action.

3. Applicant's election with traverse of Group II, filed 03/02/2006, is acknowledged. The traversal is on the ground that search and examination of the antibody of Group II and polypeptide of Group I together would not be undue burden. This is not found persuasive because Groups I and II are different products with distinct structures, physicochemical properties and/or mode of action.

In addition, antibody and polypeptide do not share a common structure that is disclosed to be essential for common utility; therefore, each product is patentably distinct and searching of these inventions would impose an undue burden.

Consequently, the restriction is still deemed proper and is therefore made FINAL.

Claims 4-14 have been canceled.
Claims 1-3 have been amended.
Claims 15-29 have been added.

Claims 1-3, 15-29 are pending.

Claims 1, 2, 28, and 29 are withdrawn from further consideration by the Examiner, under 37 C.F.R. 1.142(b), as being drawn to nonelected inventions.

Claims 3, 15-27, read on an isolated antibody that selectively binds to polypeptide of SEQ ID NO:2 and a composition comprising the antibody, are currently under consideration.

4. Applicant's claim for domestic priority under 35 U.S.C. 121 is acknowledged. The priority application 09/820,004 upon which benefit is claimed appears to provide adequate support under 35 U.S.C. 112 for subject matter claimed in the instant application.

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 121, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

The specification on page 1, line one should be amended to reflect the status of the priority application 09/820,004, which is now US Patent 6,649,385.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

6. Applicant's IDS, filed 05/18/2005, is acknowledged. Applicant's submission of Search Report on IDS is acknowledged, however, this citation has been crossed out as it is not appropriate for printing on an issued US Patent.

7. The specification is objected to for failing to provide a brief description of each individual Figure. Figures 1-3 consist of separate drawing panels each, which must be separately labeled and individually described. For example, Figure 1, which has panels labeled 1A and 1B must be identified in the Description of the Figure Sheet as "Figures 1A and 1B", after which each individual panel must be separately described. Appropriate correction is required.

8. The application is required to be reviewed and all spelling, TRADEMARK, and like error corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent application, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 18-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18-21 are indefinite in the recitation of "the antibody". There is insufficient antecedent basis for this limitation in this claim. The independent claims 3 and 15 recite "an isolated antibody" not a conjugated/coupled antibody.

Applicant is suggested to amend the preamble of claims 18-21 to include "conjugated antibody" and recite the detectable substance accordingly.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

Applicant is required to identify the written support for claims 22-25, particularly the claimed limitation of "pharmaceutically acceptable carrier".

Alternatively, applicant is invited to amend the specification to provide antecedent basis for the claimed subject matter.

13. Claims 15, 17, 19, 21, 23 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 15, 17, 19, 21, 23 and 27 recite "polypeptide comprises SEQ ID NO:2" as part of the invention.

The specification does not provide sufficient enabling description of the claimed invention. The specification discloses only protein with amino acid sequence of SEQ ID NO:2. However, the term "comprise" in the claims are open-ended; it expands the sequence of SEQ ID NO:2 to include additional non-disclosed amino acid residues outside of the sequence shown in SEQ ID NO:2.

In addition, the instant specification on page 7 discloses that a protein of SEQ ID NO:2 comprises the peptide or additional amino acid molecules from few amino acid residues to several hundred or more residues. Therefore, the instant claims encompass in their breadth any proteins "comprising" amino acid sequence disclosed in SEQ ID NO:2 and additional unknown amino acid residues.

Neither does the specification provide a sufficient enabling description of an antibody reactive towards a genus of a "polypeptide comprises SEQ ID NO:2".

Coleman et al. (Research in Immunology, 1994; 145(1): 33-36) teach that single amino acid changes in an antigen can effectively abolish antibody antigen binding (see entire document, particularly page 34). Abaza et al. (Journal of Protein Chemistry, Vol. 11, No. 5, 1992, pages 433-444) teach that single amino acid substitutions outside the antigenic site on a protein effect antibody binding (see entire document, particularly Results on pages 435-436).

Furthermore, in addition to the lack of sufficient enabling description of the claimed genus of the "polypeptide comprises SEQ ID NO:2", Applicant has not provided a sufficient enabling description of an antibody that selectively binds to such polypeitde, because such antibody would not reasonably be expected to be reactive with the "polypeptide comprises SEQ ID NO:2", and therefore to be functional. For example, Lederman et al. (Molecular Immunology 1991. 28: 1171-1181. See entire document) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody. Further, Li et al. (PNAS 1980. 77: 3211-3214. See entire document) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document). Therefore, the specification does not provide for sufficient enablement for antibodies reactive with "polypeptide comprises SEQ ID NO:2".

Thus the structure of claimed antibodies cannot be readily envisioned by one of skill in the art based upon the guidance provided in the specification as-filed. Therefore, Applicant does not provide a sufficiently enabling disclosure regarding how to make and use an antibody to the genus of "polypeptide comprises SEQ ID NO:2".

In view of the lack of predictability of the art to which the invention pertains, working examples, the state of the art teachings, undue experimentation would be required to practice the claimed invention.

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 3, 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Robinson (US Patent 5,589,372 cited in IDS filed 05/18/2005) as evidenced by Bost et al. (Immunol. Invest. 1988; 17:577-586) (see entire document) and Bendayan (J. Histochem. Cytochem. 1995; 43:881-886) (see entire document).

Robinson teaches isolated polypeptide of squalene synthetase comprising an amino acid sequence of SEQ ID NO:6 that shares 98.4% homology of polypeptide with amino acid sequence of SEQ ID NO:2 of the instant claims (see entire document, particularly columns 2-11 and claim 1). Robinson further teaches that antibodies capable of binding the squalene synthetase with amino acid of SEQ ID NO:6 such as monoclonal antibody can be made (e.g. see column 11, in particular).

As evidenced by Bost et al, antibodies can be specific and cross-react with the antigen. For example, antibodies which "cross-react" with IL-2 and HIV envelope protein, but establish that the binding of each protein is due to the presence of a homologous sequence in each protein in which 4 of 6 residues were identical (see entire document, but especially the Abstract and Discussion). Antibodies which bound either the HIV or IL-2 derived sequence did not cross-react with irrelevant peptides (e.g., "Results, page 579).

As further evidenced by Bendayan, the specific reactivity of a monoclonal antibody can be highly specific yet cross-react with antigens from different species or even distinct proteins not related to the original antigen (page 886, last paragraph).

Given the high degree of sequence homology between the prior art squalene synthetase of SEQ ID NO:6 and instant polypeptide comprising SEQ ID NO:2, monoclonal antibody that binds to the prior art synthetase would bind shared regions of sequence identity of the instant polypeptide comprising SEQ ID NO:2.

Therefore, the reference teachings anticipate the claimed invention.

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 3 and 15-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robinson (US Patent 5,589,372 cited in IDS filed 05/18/2005) in view of Bost et al. (Immunol. Invest. 1988; 17:577-586), Bendayan (J. Histochem. Cytochem. 1995; 43:881-886), and Harlow et al. (Antibodies, A Laboratory Manual 1988, pages 319-358).

The teachings of Robinson have been discussed, supra, and teach that the antibodies can be used for the detection of the polypeptides with immunoassay techniques such as radioimmunoassay or enzyme immunoassay (see entire document, particularly column 11). The teachings of Bost et al. and Bendayan have been discussed, supra.

Robinson, Bost et al. and Bendayan do not teach an antibody that is coupled to a detectable substance and a pharmaceutically acceptable carrier.

However, methods of coupling antibodies to a detectable substance for immunoassay in buffers were well known in the art at the time the invention was made. For example, Harlow et al. teach methods of immunoassay using antibodies coupled directly to a detectable substance such as biotin, horseradish peroxidase (see entire document, particularly pages 340-358); such direct coupling methods provide fewer steps and are less prone to background problems (e.g. see page 321, in particular). Further, Harlow et al. teach examples of coupling antibody to detectable substance buffers such as phosphate-buffered saline (PBS), a well known pharmaceutically acceptable carrier (e.g. see page 341, in particular).

It would thus have been obvious to the ordinary artisan at the time the invention was made to couple the antibody that binds to a squalene synthetase to a detectable substance in well known carriers such as PBS for use in immunoassay. The ordinary artisan would have been motivated to couple the antibody to a detectable substance because direct coupling of antibodies to a detectable substance provide fewer steps and less background in immunoassay.

Given the teachings of Robinson, Bost et al. and Bendayan regarding the antibody specific for squalene sythetase that shares 98.4% homology with the claimed polypeptide comprising SEQ ID NO:2, and the teachings Harlow et al, regarding that coupling antibodies directly to a detectable substance provide fewer steps and less background in immunoassay, the ordinary artisan at the time the invention was made would have had a reasonable expectation success to produce antibody that binds to polypeptide of SEQ ID NO:2 coupled to a detectable substance in carriers such as PBS.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. Claims 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pluckthun et al. (Immunotechnology 1997, 3:83-105) in view of Robinson (US Patent 5,589,372 cited in IDS filed 05/18/2005), Bost et al. (Immunol. Invest. 1988; 17:577-586), and Bendayan (J. Histochem. Cytochem. 1995; 43:881-886).

Pluckthun et al. teach that recombinant antibody fragments such as Fab, $F(ab')_2$, and Fv provide improved performance in vivo and in a variety of in vitro assays (see entire document, particularly pages 93-95 and Figure 6 on page 92).

Pluckthun et al. do not teach antibody fragment that binds to polypeptide of SEQ ID NO:2.

The teachings of Robinson, Bost et al. and Bendayan have been discussed, supra.

The teachings of Robinson, Bost et al, and Bendayan have been discussed, supra.

Therefore, it would have been obvious to the ordinary artisan at the time the invention was made to make antibody fragments including Fab, $F(ab')_2$, and Fv that bind to polypeptide of SEQ ID NO:2. The ordinary artisan would have been motivated to do so because it is well know in the art at the time the invention was made to make antibody fragments for improved performance in vivo and in a variety of in vitro assays.

Given the teachings of Pluckthun et al. regarding the antibody fragments, and the teachings of Robinson, Bost et al, and Bendayan providing method and the use of antibodies that bind polypeptide of SEQ ID:2, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success producing antibody fragments such as Fab, $F(ab')_2$, and Fv that binds polypeptide of SEQ ID NO:2.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.
Patent Examiner
April 3, 2006

PHILLIP GAMBEL, PH.D JD
PRIMARY EXAMINER
TC 1600
4/5/06

Application No.: 10/644,021

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- [X] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [X] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [X] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [ ] 7. Other: _____

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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